Amendments to the Specification:

Please delete the paragraph inserted at page 1, below the title, of the specification as amended by the Preliminary Amendment of October 30, 2007 and substitute therefor:

This application is a national phase under 35 U.S.C. §371 of PCT/US2003/038582, filed December 3, 2003, which is a continuation-in-part of U.S. application Serial No. 10/309,803, filed December 3, 2002, now U.S. Patent 7,611,869, issued November 3, 2009, both of which are [[re]] incorporated by reference in their entirety.

Please delete the paragraph starting on page 2, line 7 and substitute therefor:

Recent focus has been on the analysis of the relationship between genetic variation and phenotype by making use of polymorphic DNA markers. Previous work utilized short tandem repeats (STRs) as polymorphic positional markers; however, recent focus is on the use of single nucleotide polymorphisms (SNPs), which occur at an average frequency of more than 1 per kilobase in human genomic DNA. Some SNPs, particularly those in and around coding sequences, are likely to be the direct cause of therapeutically relevant phenotypic variants and/or disease predisposition. There are a number of well known polymorphisms that cause clinically important phenotypes; for example, the apoE2/3/4 variants are associated with different relative risk of Alzheimer's and other diseases (see ~~Corder~~ Corder et al., Science 261:921-923 (1993). Multiplex PCR amplification of SNP loci with subsequent hybridization to oligonucleotide arrays has been shown to be an accurate and reliable method of simultaneously genotyping at least hundreds of SNPs; see Wang et al., Science, 280:1077 (1998); see also Schafer et al., Nature Biotechnology 16:33-39 (1998). However, in Wang et al. only 50% of 558 SNPs were amplified successfully in a single multiplexed amplification reaction. As such, there exists a need for methods that increase the fidelity and robustness of multiplexing assays.

Please delete the paragraph starting on page 18, line 20 and substitute therefor:

In a preferred embodiment, the compositions and methods of the invention are directed to the detection of target sequences. By "nucleic acid" or "oligonucleotide" or grammatical equivalents herein [[ ]]means at least two nucleotides covalently linked together. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, as

outlined below, particularly for use with probes or primers, nucleic acid analogs are included that may have alternate backbones, comprising, for example, phosphoramide (Beaucage et al., Tetrahedron 49(10):1925 (1993) and references therein; Letsinger, J. Org. Chem. 35:3800 (1970); Sprinzl et al., Eur. J. Biochem. 81:579 (1977); Letsinger et al., Nucl. Acids Res. 14:3487 (1986); Sawai et al, Chem. Lett. 13:805-808 (1984), Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); and Pauwels et al., Chemica Scripta 26:141 91986)), phosphorothioate (Mag et al., Nucleic Acids Res. 19:1437 (1991); and U.S. Patent No. 5,644,048), phosphorodithioate (Briu et al., J. Am. Chem. Soc. 111:2321 (1989), O-methylphosphoroamidite ~~O-methylphophoroamidite~~ linkages (see Eckstein, Oligonucleotides and Analogues: A Practical Approach, Oxford University Press), and peptide nucleic acid backbones and linkages (see Egholm, J. Am. Chem. Soc. 114:1895 (1992); Meier et al., Chem. Int. Ed. Engl. 31:1008 (1992); Nielsen, Nature, 365:566 (1993); Carlsson et al., Nature 380:207 (1996), all of which are incorporated by reference). Other analog nucleic acids include those with positive backbones (Denpcy et al., Proc. Natl. Acad. Sci. USA 92:6097 (1995); non-ionic backbones (U.S. Patent Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowshi et al., Angew. Chem. Intl. Ed. English 30:423 (1991); Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); Letsinger et al., Nucleoside & Nucleotide 13:1597 (1994); Chapters 2 and 3, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y.S. Sanghui and P. Dan Cook; Mesmaeker et al., Bioorganic & Medicinal Chem. Lett. 4:395 (1994); Jeffs et al., J. Biomolecular NMR 34:17 (1994); Tetrahedron Lett. 37:743 (1996)) and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y.S. Sanghui and P. Dan Cook. Nucleic acids containing one or more carbocyclic sugars are also included within the definition of nucleic acids (see Jenkins et al., Chem. Soc. Rev. (1995) pp169-176). Several nucleic acid analogs are described in Rawls, C & E News June 2, 1997 page 35. All of these references are hereby expressly incorporated by reference. These modifications of the ribose-phosphate backbone may be done to facilitate the addition of labels, or to increase the stability and half-life of such molecules in physiological environments.

Please delete the paragraph starting on page 60, line 27 and substitute therefor:

Other preferred configurations of the system are set forth in U.S.S.N.s 10/177,727, filed June 20, 2002, now published U.S. application 2003/0211489 and 10/194,958, filed July 12, 2002, now U.S. Patent 7,582,420, both of which are expressly incorporated herein by reference.

Please delete the paragraph starting on page 69, line 23 and substitute therefor:

The ligation of the extended first probe and the second probe results in an amplification template comprising at least one, and preferably two, universal primers and an optional adapter. Amplification can then be done, in a wide variety of ways. As will be appreciated by those in the art, there are a wide variety of suitable amplification techniques requiring either one or two primers, as is generally outlined in U.S.S.N. 09/517,945, now U.S. Patent 6,355,431, hereby expressly incorporated by reference.

Please delete the paragraph starting on page 71, line 8 and substitute therefor:

Accordingly, the present invention provides array compositions comprising at least a first substrate with a surface comprising individual sites. By "array" or "biochip" herein is meant a plurality of nucleic acids in an array format; the size of the array will depend on the composition and end use of the array. Nucleic acids arrays are known in the art, and can be classified in a number of ways; both ordered arrays (e.g. the ability to resolve chemistries at discrete sites), and random arrays are included. Ordered arrays include, but are not limited to, those made using photolithography techniques (Affymetrix GeneChip™), spotting techniques (Synteni and others), printing techniques (Hewlett Packard and Rosetta), three dimensional "gel pad" arrays, etc. A preferred embodiment utilizes microspheres on a variety of substrates including fiber optic bundles, as are outlined in PCTs US98/21193, now published international application WO99/18434, PCT US99/14387, now published international application WO99/67641 and PCT US98/05025, now published international application WO99/67641; WO98/50782; and U.S.S.N.s 09/287,573, now U.S. Patent 7,348,181, 09/151,877, now U.S. Patent 6,327,410, 09/256,943, now U.S. Patent 6,429,027, 09/316,154, now U.S. Patent 6,364,790, 60/119,323, 09/315,584, now U.S. Patent 6,544,732; all of which are expressly incorporated by reference.

Please delete the paragraph starting on page 73, line 7 and substitute therefor:

In a preferred embodiment, the substrate is an optical fiber bundle or array, as is generally described in U.S.S.N.s 08/944,850, now U.S. Patent 7,115,884, and 08/519,062, now U.S. Patent 6,200,737, PCT US98/05025, now published international application WO98/40726, and PCT US98/09163, now published international application WO98/50782, all of which are expressly incorporated herein by reference.[[.]] Preferred embodiments utilize preformed unitary fiber optic arrays. By "preformed unitary fiber optic array" herein is meant an array of discrete individual fiber optic strands that are co-axially disposed and joined along their lengths. The fiber strands are generally individually clad. However, one thing that distinguished a preformed unitary array from other fiber optic formats is that the fibers are not individually physically manipulatable; that is, one strand generally cannot be physically separated at any point along its length from another fiber strand.

Please delete the paragraph starting on page 73, line 16 and substitute therefor:

Generally, the array of array compositions of the invention can be configured in several ways; see for example U.S.S.N. 09/473,904, now U.S. Patent 6,858394, hereby expressly incorporated by reference. In a preferred embodiment, as is more fully outlined below, a "one component" system is used. That is, a first substrate comprising a plurality of assay locations (sometimes also referred to herein as "assay wells"), such as a microtiter plate, is configured such that each assay location contains an individual array. That is, the assay location and the array location are the same. For example, the plastic material of the microtiter plate can be formed to contain a plurality of "bead wells" in the bottom of each of the assay wells. Beads containing the capture probes of the invention can then be loaded into the bead wells in each assay location as is more fully described below. Arrays are described in U.S. Patent No. 6,023,540 and U.S.S.N.'s 09/151,877, filed September 11, 1998, now U.S. Patent 6,327,410, 09/450,829, filed November 29, 1999, now U.S. Patent 6,266,459, 09/816,651, filed March 23, 2001, now abandoned, and 09/840,012, filed April 20, 2001, now abandoned, all of which are expressly incorporated herein by reference. In addition, other arrays are described in 60/181,631, filed February 10, 2000, 09/782,588, filed February 12, 2001, now abandoned, 60/113,968, filed December 28, 1998, 09/256,943 ~~090/256,943~~, filed February 24, 1999, now U.S. Patent 6,429,027, 09/473,904, filed December 28, 1999, now U.S. Patent 6,858394 and 09/606,369, filed June 28, 2000, now abandoned, all of which are expressly incorporated herein by reference.

Please delete the paragraph starting on page 73, line 7 and substitute therefor:

In a preferred embodiment, the substrate is an optical fiber bundle or array, as is generally described in U.S.S.N.s 08/944,850, now U.S. Patent 6,023,540 and 08/519,062, now U.S. Patent 6,327,410, PCT US98/05025, now published international application WO98/040726, and PCT US98/09163, now published international application WO98/050782, all of which are expressly incorporated herein by reference.[[.]] Preferred embodiments utilize preformed unitary fiber optic arrays. By "preformed unitary fiber optic array" herein is meant an array of discrete individual fiber optic strands that are co-axially disposed and joined along their lengths. The fiber strands are generally individually clad. However, one thing that distinguished a preformed unitary array from other fiber optic formats is that the fibers are not individually physically manipulatable; that is, one strand generally cannot be physically separated at any point along its length from another fiber strand.

Please delete the paragraph starting on page 79, line 14 and substitute therefor:

However, the drawback to these methods is that for a large array, the system requires a large number of different optical signatures, which may be difficult or time-consuming to utilize. Accordingly, methods for analysis and decoding of arrays are described in 08/944,850, filed October 6, 1997, now U.S. Patent 7,115,884, PCT/US98/21193, filed October 6, 1998, now published international application WO99/18434, 09/287,573, filed April 6, 1999, now U.S. Patent 7,348,181, PCT/US00/09183, filed May 6, 2000, now published international application WO00/60332, 60/238,866, filed October 6, 2000, 60/119,323, filed February 9, 1999, 09/500,555, filed February 9, 2000, now abandoned, 09/636,387, filed August 9, 2000, now abandoned, 60/151,483, filed August 30, 1999, 60/151,668, filed August 31, 1999, 09/651,181, filed August 30, 2000, now U.S. Patent 6,942,968, 60/272,803, filed March 1, 2001, all of which are expressly incorporated herein by reference. In addition, methods of decoding arrays are described in 60/090,473, filed June 24, 1998, 09/189,543, filed November 10, 1998, now abandoned, 09/344,526, filed June 24, 1999, now U.S. Patent 7,060,431, PCT/US99/14387, filed June 24, 1999, now published international application WO99/67641, 60/172, 106, filed December 23, 1999, 60/235,531, filed September 26, 2000, 09/748,706, filed December 22, 2000, now U.S. Patent 7,033,754, and provisional application entitled Decoding of Array

Sensors with Microspheres, filed June 28, 2001 (no serial number received), all of which are expressly incorporated herein by reference.